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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/535,709	05/20/2005	Jens Damsgaard Mikkelsen	2815-0316PUS1	7585

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BIRCH STEWART KOLASCH & BIRCH
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FALLS CHURCH, VA 22040-0747

EXAMINER

CORNET, JEAN P

ART UNIT	PAPER NUMBER
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1614

NOTIFICATION DATE	DELIVERY MODE
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10/07/2009

ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

mailroom@bskb.com

Office Action Summary	Application No. 10/535,709	Applicant(s) MIKKELSEN, JENS DAMSGAARD	
	Examiner JEAN CORNET	Art Unit 1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 27 July 2009.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-5 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-5 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

** ?? What is the "na" superscript over the "2" in the next two headers??

Rejections under 35 U.S.C. §112~ 2^{na} paragraph

1. Applicant's arguments, see page 3, filed 07/27/2009, with respect to the rejection under 35 U.S.C., second paragraph have been fully considered and are persuasive. The rejection of claims 1 and 5 has been withdrawn.

Rejections under 35 U.S.C. §112~ 2^{na} paragraph

2. Applicant's arguments that Kuo-Fen and Barbaccia fail to teach that compound, which substantially stimulates the HPA axis can be selected as a sedative drug candidate and that a compound, which substantially has no effect on the HPA axis, can be as an anxiolytica drug candidate have been fully considered but they are not persuasive. The combined references Kuo-Fen and Barbaccia would be clearly evident to one skilled in the art to apply the features of Barbaccia with corresponding effect to the known screening method of Kuo-Fen to come to the solution proposed Applicant as stated in the office action.

3. Applicant's arguments filed 07/27/2009 have been fully considered. Rejections and objections not reiterated form previous Office Action are hereby withdrawn. The following rejections are either reiterated or newly applied. They

Art Unit: 1614

constitute the complete set of rejections presently being applied to the instant application due to claims amendment.

Claim Rejections - 35 USC § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1-5 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kuo-Fen et al (WO0105222) in view of Barbaccia (Stress and Neurosteroids in Adult and Aged Rats, Experimental Gerontology, Vol 33, Nos 7/8, pp. 697-712, 1998), both cited in the IDS.

The instant application is drawn to a method of screening a GABA_A receptor modulator for its potential as a sedative or anxiolytica, which comprises exposing the compound to a test animal by administration; and measuring the effect of the compound on the activity of the HPA axis.

Art Unit: 1614

As to claim 1-3, Kuo-Fen et al teaches a method for screening for compounds having an effect on the response of the hypothalamic-pituitary-adrenal axis (HPA) to stress, comprising the steps of

- a) administering said compound to a transgenic mouse with a disruption in at least one allele of the corticotrophin releasing factor receptor 2 (CRFR2),
- b) putting the said mouse in a stress-inducing situation,
- c) monitoring plasma levels of corticosterone and adrenocorticotrophic hormone (ACTH) in the mouse after administration, and d) comparing said levels to those said transgenic mouse not placed in a stress-inducing conditions (claim 12).

Compounds having a sedative effect in this model will induced less stress response in terms of increase corticosterone or ACTH release which are components of the HPA axis activity (example 5).

Although the instantly claimed invention differs in that the compounds have to be modulators of the GABA_A receptor, It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to substitute a GABA_A receptor modulator when Kuo-Fen is taking in view of Barcaccia et al, Barbaccia suggests that modulators of GABA_A receptors affect correspondingly the HPA axis and the behavioral correlates to acute stress (abstract), thus remedies the deficiency of Kuo-Fen.

One would have been motivated to do so, with reasonable expectation of success because barcaccia's teaching clearly suggests that the substitution would have been equivalent. The techniques and skill required to such substitution is conventional knowledge or well within the skill of ordinary artisan.

Art Unit: 1614

Kuo-Fen does not teach selecting the compound as a sedative drug candidate if the compound substantially stimulates the HPA axis as in claim 4 and selecting the compound as an anxiolytica drug candidate, if the compound substantially has no effect on the HPA axis as in claim 5.

As to claims 4 and 5, Barbaccia et al teaches modulators of GABA_A receptors affect the HPA axis and the behavior correlates of acute stress (page 698 first paragraph and page 710 second paragraph). Barbaccia further teaches contrary to inhibitors, activators prevent the activation of the HPA axis, i.e reduce the plasma and brain neurosteroid, and induce less stress response. Modulators of GABA_A receptors are generally known as anxiolitics and hypnotics (abstract)

Since Applicant defines in the specification, page 3, lines 22-35 that an increase in corticosterone and/or ACTH plasma level is an indication that the compound stimulates the HPA axis thereby can be selected as a sedative drug candidate and a decrease in the corticosterone and/or ACTH plasma level is an indication that the compound has substantially no effect on the HPA axis, thereby can be selected as anxiolytica drug candidate; and since Kuo-Fen teaches compounds having a sedative effect in this model will induced less stress response in terms of increase corticosterone or ACTH release which are components of the HPA axis activity and Barbaccia teaches contrary to inhibitors, activators prevent the activation of the HPA axis, i.e reduce the plasma and brain neurosteroid, and induce less stress response. Modulators of GABA_A receptors are generally known as anxiolitics and hypnotics, It would have been prima facie obvious to one of ordinary skill in the art to combine the features of Barbarccia's

Art Unit: 1614

reference with corresponding effect to the known screening method of Kuo-Fen to come to the solution proposed by the instantly claimed application by selecting compounds either as sedative drugs or anxiolytica drugs.

Conclusion

5. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to JEAN CORNET whose telephone number is (571)270-7669. The examiner can normally be reached on Monday-Thursday 7.00am-5.30pm.

Art Unit: 1614

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel can be reached on 571-272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/JC/

/Ardin Marschel/
Supervisory Patent Examiner, Art Unit 1614